Biocatalytic and Biomimetic Generation of Nitric Oxide *in situ* at Substrate/Blood Interfaces

ABSTRACT OF THE DISCLOSURE

Biocompatible materials that have the ability to release nitric oxide (NO) *in situ* at the surface-blood interface when in contact with blood. The materials which may be polymers (*e.g.*, polyurethane, poly(vinyl chloride), silicone rubbers), metals, such as stainless steel, carbon, and the like are provided with biocatalysts or biomimetic catalysts on their surface that have nitrite, nitrate, and/or nitrosothiol-reducing capability. Illustratively, the catalysts are adsorbed or immobilized at the surface of the material. The catalysts can act on endogenous nitrite, nitrate, or nitrosothiols within the blood creating a local increase in the NO levels at the surface of the material. An illustrative enzymatic biocatalyst is mammalian xanthine oxidase. In another illustrative embodiment, a biomimetic catalyst is a copper (Cu(II)-ligand complex, *e.g.* dibenzo[e,k]-2,3,8,9-tetraphenyl-1,4,7,10-tetraaza-cyclododeca-1,3,7,9-tetraene. In some cases, lipophilic salts of nitrite/nitrate (*e.g.*, tridodecylmethylammonium nitrite ($TDMA^+$ NO_2^- /NO_3^-)) or certain salts of nitrosothiols can be doped within a polymer material, or an underlying polymeric film, to create a reservoir of nitrite or nitrosothiol that continuously leaks into the immobilized catalytic layer. Adequate levels of endogenous reducing equivalents are present within blood to provide catalytically-generated surface levels of NO that are above the threshold reportedly required to prevent platelet adhesion or activation.